UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/674,819 | 11/06/2000 | Akira Aomatsu | 5774-01-MJA | 5038 |

7590 09/26/2003

Charles W Ashbrook
Warner Lambert Company
2800 Plymouth Road
Ann Arbor, MI 48105

| EXAMINER |
|---|
| KIM, VICKIE Y |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1614 | 16 |

DATE MAILED: 09/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/674,818 | Applicant(s) LEOPOLD ET AL. | |
|---|---|---|---|
| | Examiner Vickie Kim | Art Unit 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-17 and 20-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 20-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Request for the Continued examination(RCE) acknowledged*

1. The request filed on 04/20/2003 for a RCE under 37 CFR 1.114 based on parent Application No. 09/674819 is acceptable and a RCE has been established. An action on the RCE follows.

### *Status of Application*

Acknowledgement is made of amendment filed 04/20/2003. As requested, claims 22-27 are added. The claims 1-17 and 20-27 are pending, and presented for the examination.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 6, 13, 23 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term " **lower** " right before "aliphatic acid ester of glycerol" in claims 6, 13, 23 and 26 is a relative term which renders the claim indefinite. The term "lower" is not defined by the claim, or is lacking a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Clarification is required.

### *Claim Rejections - 35 USC § 102/103*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 10-12, 14, 22, 25 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Augart et al (US'6,054,482) in view of US5302373, Telev(1982, abstract), US5618342 and/or BE645388.

Augart et al(US'482, hereafter) teach a stable solid composition in the form of tablet or capsules(dry medicinal forms) and a process for the preparation thereof, wherein the composition comprises a cyclic amino derivative of the general formula I such as gabapentin as an active agent and an adjuvant materials (e.g. polyvinylpyrrolidone, cyclodextrin, lactose, talc , polyethylene glycol), see abstract, col. 2, lines 27-30, claims (especially, claim 4, (c) and claim 8) and column 3 lines 25-45. It

is noted that the specific adjuvants of US'482(i.e. polyvinylpyrrolidone, cyclodextrin, lactose, talc and polyethylene glycol) are conventionally known as humectants and naturally play the role as "humectant" that is any substance added to another substance to keep the moisture. The said adjuvants of US'482 are, thus, inherently possess the feature required by the instant claims. Any compound of the said adjuvants of US482 would be used to prevent the excess water available for forming undesirable lactam. Thus, the claims are met by the cited reference because the said adjuvant compounds(e.g polyvinylpyrrolidone, cyclodextrin, lactose, talc , polyethylene glycol) carry out the stabilization of the active agent from lactam formation whether they are called humectant or not.

For instance, the stabilizing activity carried out by the said adjuvants is enabled in US'482 wherein the formation of lactam (byproduct) that is usually associated with certain toxicities can be suppressed by the preferred adjuvants (e.g. polyvinylpyrrolidone, cyclodextrin, lactose, talc , polyethylene glycol, see column 4, lines 60 thru column 5, lines 33.

Thus, these broadly drafted claims that are drawn to a solid composition comprising a 4-amino-3-substituted-butanoic acid derivative such as gabapentin(active agent) and a stabilizer(being a humectant) effective against degradation of the active agent due to lactam formation, are readily envisioned and anticipated by the cited reference.

All the critical elements required by the instant claims are well taught by the cited reference.

Or in alternatively, the claims 1, 8, 10, 11, 12, 14, 22, 25 are rejected under 35 U.S.C. 103(a) as obvious over Augart et al(US'482) in view of numerous evidentiary documents cited in PTO-892 including US5302373, Telev(1982, abstract), US5618342 and/or BE645388.

Even if applicants traverse this examiner's allegation because humectant is silent in US'482, paraphrasing of this, even if applicants traverse inherent activity of the said adjuvants as the humectant, the claims 1, 8, 10, 11, 12, 14, 22, 25 are still rejected as obvious, because the fact that the adjuvants (e.g. polyvinylpyrrolidone, cyclodextrin, lactose, talc , polyethylene glycol) are the humectant is not only conventionally acknowledged but also evidenced by numerous documents including US5302373, Telev(1982, abstract), US5618342 and/or BE645388(abstract), for instance.

US'373 teaches that propylene glycol, glycerol, sorbitol, or cyclodextrin is functionally equivalent humectant, see column 2, lines 28-33.

US'342 teaches that glycerol, substituted glycerol, sorbitol, polyethylene glycol, polypropylene glycol, polyvinylpyrrolidone is functional equivalent humectant, see claim 3.

Telev(abstract) teaches a polyethylene glycol has stronger humectant activity than sorbitol, glycerol, or propylene glycol.

BE'388(abstract) teaches that polyethylene glycol, ethylene glycol or glycerol is functionally equivalent humectant that improves wettability or film-forming properties.

When the teaching of each reference(individually or in combination) is taken together with US'482, it would have been readily apparent to the one of ordinary skill in

the art to envision the term substitution where the adjuvants can be substituted with the term ,humectant where polyvinylpyrrolidone, cyclodextrin, lactose, talc or polyethylene glycol is effectively preventing the lactam formation via suppressing catalysis as suggested by US'482 at column 4 and claim 3(c).

One would have motivated to do so , with reasonable expectation of success, because the humectants(i.e polyvinylpyrrolidone, cyclodextrin, lactose, talc or polyethylene glycol ) can effectively absorb the excessive water that is required for the lactam formation so that the water would not be available for lactam formation.

One would have been motivated to modify the reference and have expected reasonable success, because they are drawn to same technical fields (constituted with same ingredients(e.g. polyvinylpyrrolidone, cyclodextrin, lactose, talc , polyethylene glycol ) and share common utilities(i.e. activity of the humectant to suppress lactam formation) , and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

7. Claims 1,2,7-14, 22, 25 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Cherukuri et al(EP 0458751).

The claims are drawn to a solid composition comprising 4-amino-3-butanoic acid derivatives of the formula claimed and a stabilizer, the stabilizer being humectant and effective against degradation.

EP'751 teaches a composition , especially in the tablet form, comprising cyclic amino acid compounds having the general formula such as gabapentin(see page 4); and an excipients such as polyvinylpyrrolidone(disintergrating agent or binder, see page

7, lines 5 and 33) or sorbitol(diluent, see pages 6, lines 55 thru page 7, lines 33 and 39) in addition to other auxiliary agents such as lubricants, glidants, etc (see page 7). EP'751 further teaches that the patented delivery system using said excipients provide improved integrity and shelf life , effective physicochemical changes as well as stability of tablet configuration, see from page 6, lines 55-page 7, lines 39(bridged).

Therefore, EP'751 teaches all the critical elements required by the instant claims wherein the composition of EP' 751 and the preparation thereof include gabapentin(same active agent as required by the instant claims) and the stabilizer being humectant such as sorbitol or a polyvinylpyrrolidone.

As mentioned immediately above in 102/103 rejection (Augart et al, US'482) (supra), the claims are rejected under 102/103 because the said excipeints(i.e. sorbitol, polyvinylpyrrolidone) inherently exhibit the activity as a humectant. For the very same reason mentioned above, the inherency plays role in this rejection where sorbitol or polyvinylpyrrolidone is naturally functioning as humectant and stabilizing the active agent by suppressing lactam formation whether these compounds are called by the term, humectant or not.

Again, the allegation of this examiner can be supported by incorporating numerous evidentiary documents that are cited in PTO-892 and applicants own admission at pages 44-47 where applicant also acknowledges multi-functionalities of the ingredients required by the claims, for example, at page 44, applicants state that sorbitol is humectant but also exhibit an activity as a sweetening agent. At page 47, applicants also state that propylene glycol, glycerol and triacetin are acting not only as

a humectant but also as a plasticizer. Thus, the composition of EP'571 comprising gabapentin and polyvinylpyrrolidone in an effective amount about 5%-15%, and the preparation thereof are well encompassed by the scope of the instant claims.

It is noted that the instant claims are directed to the composition claims not to a method claims. *A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.* Because all the critical elements including the amount of each elements are well taught by the cited reference, the claimed subject matter is not patentably distinguished from the teaching of the cited reference under 102 rejection. Even if there is some ambiguities due to the multi-functionalities of the said excipients(e.g. sorbitol or polyvinylpyrrolidone) where they are called in different name such as diluent, binder, disintergrating agent, the ambiguities is simply overcame by incorporating the conventional knowledge because their inherent characteristics as a humectant is conventionally known and widely used by any skilled or ordinary skilled artisan in the art as evidenced by numerous documents(see PTO-892).

8. Claims 1,7-17, 20-21 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Robson et al(US 4,126,684).

US'684 teaches a solid pharmaceutical composition(e.g. tablets, capsules or suppositories) comprising baclofen(4-amino-3-halophenylbutyric acid), an effective

amount of a pharmaceutical excipient(e.g. sorbitol, mannitol, lactose, polyvinylpyrrolidone), a neutral amino acid(i.e. glycine) and other auxiliary agent such as colorants, flavors, and sweeteners, see abstract, column 3, lines 54-69 and examples. The amount of humectant included would be calculated simply by basic calculation, for example, the amount of lactose in example 1 is about 5%. Thus, the limitations recited in the instant claims 8-9 are encompassed by the teaching of the cited reference. Especially, US'684 contemplates patented composition comprising baclofen, mannitol, glycine and saccharin at example 2. As mentioned in other 102/103 rejection above(supra), sorbitol, mannitol or lactose is classified differently due to its multi-functionalities and used in pharmaceutical field with different names. However, the said compounds are the humectant inherently where it naturally stabilizes the active agent by suppressing the lactam formation. And thus, all the claims are not patentably distinct over the prior art of the record.

For the very same reason mentioned above(US'482 or EP571), the instant claims are rejected under 102/103 as being anticipated by or in alternatively, obvious over US'684.

9. Claims 1-7, 10-15, 20-27 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Wallace (US 5,025,035).

Wallace et al(US'035, hereafter) teaches a solid pharmaceutical composition in the form of tablet or capsule, which comprising a compound of general formula I(e.g. 1-aminomethyl-1-cyclohexane acetate) and a pharmaceutical carrier such as propylene

glycol, glycerin, sorbitol, or polyethylene glycol in addition to other auxiliary agents such as flavoring agents and/or preservatives, see column 2.

As to the claims 2-4, 6-7, 13, 23-24 and 26-27, US'035 teaches propylene glycol, glycerin(chemical name:glycerol) and sorbitol. Thus, all the critical elements are taught and the claims are included in this rejection.

Thus, for the very same reason mentioned earlier in 102/103 rejection(US'482, EP'571 or US'684), all the claimed subject matter is anticipated by or in alternatively, obvious over US'482 and the instant claims are rejected under 102/103.
It is noted that the minor variations including the selection of optimal dosages, routes of administration, or variable applications in order to determine the most effective treatment is well within the skilled level of artisan having ordinary skill in the art, and is obvious.

As to claim 4 that requires butylene glycol, it is considered to be obvious variants with other humectants (e.g. propylene glycol, glycerol, sorbitol) as evidenced by the record showing the species are obvious variants as admitted by applicants during restriction/election practice, see paper 7.

Thus, all the claims are properly include in this rejection.

***Response to the argument:*** ***A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use***

***must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963).***

**Conclusion**

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 703-305-1675. The examiner can normally be reached on Tuesday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on 703-308-4725. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-3165 for regular communications and 703-746-3165 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Vickie Kim,
Patent examiner
September 19, 2003
Art unit 1614